$x = 2, y = 1$. Using the tangent-chord process (of Euler) we obtain a sequence of rational solutions $x = p_m/q_m$, $y = r_m/s_m$ $(1 \leq m \leq t)$ of $x^3 - y^3 = 7$, where t is as large as we please. Then $7 \prod_{m=1}^{t} (q_m, s_m)^3$ has at least t representations by the form $x^3 - y^3$. The notation (a, b) means the least common multiple of a and b.

[1] Here $\phi(x, y)$ is a cubic form (coefficients in Z).

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*CHROMOSOME STRUCTURE IN PHAGE T4, I. CIRCULARITY OF THE LINKAGE MAP**

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On extraction, particles of phage T4 each yield a single DNA molecule;[1-3] and in genetic crosses, all the markers prove to be linked to one another.[4] Crossing also generates short heterozygous regions that are distributed randomly over the genome.[5]

Doermann and Boehner[6] have suggested that at least some of the heterozygous regions involve interruptions of some sort in the DNA chain. Berns and Thomas[7] and Cummings,[8] on the other hand, interpret results of their experiments on the physical properties of T4 DNA to mean that the single strands are continuous.[9]

The paradox could be resolved by making two assumptions about the chromosome of phage T4. First, that it is a linear molecule with a terminal redundancy:

a b c d e f.....w x y z a b c

Second, that after several rounds of replication the chromosome becomes circularly permuted as a result of genetic recombination within the region of redundancy.[10] The ends of a population of chromosomes would thus be randomly distributed over the genome:

g h i j k l.....c d e f g h i

m n o p q r.....i j k l m n o, etc.

One of several predictions of the above model is that the linkage map of phage T4 would be circular. A test of this prediction forms the substance of the present communication.

Materials and Methods.—The phage strains used were derivatives of T4D containing the markers *r*73;[4] *tu*41, *tu*42b, *tu*44, *tu*45a, and *r*48;[11] *h*42;[12] *ac*41;[13] *r*EDb-48;[14] *am*85 and *am*54, obtained from Dr. R. H. Epstein; and *r*67, obtained from Dr. A. H. Doermann. The bacterial strains were *Escherichia coli* B, S/6, K12(λ), CR63, and K12(λ)/4.

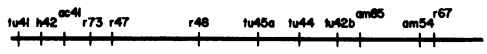

FIG. 1.—A provisional map of T4 showing the relative locations of several markers.

Media: Broth—1 liter H_2O, 10 gm bacto-tryptone, 5 gm NaCl. Tryptone plates—bottom layer, broth with 1.1 per cent bacto-agar; top layer, broth with 0.7 per cent bacto-agar. EHA plates—bottom layer contained 1 liter H_2O, 13 gm bacto-tryptone, 2 gm sodium citrate · 2 H_2O, 1.3 gm glucose, 14 gm bacto-agar, 8 gm NaCl; top layer contained 1 liter H_2O, 13 gm bacto-tryptone, 2 gm sodium citrate · 2 H_2O, 3 gm glucose, 7 gm bacto-agar, 8 gm NaCl. Salt-poor EHA plates—bottom layer was identical to EHA but contained only 2.5 gm NaCl per liter; top layer contained no added NaCl.

Acriflavin-neutral (Nutritional Biochemicals Corp.) was added, when required, to the bottom layer only, at a concentration of 0.25 μg per ml.

Results.—A linkage map of phage T4 is shown in Figure 1. With the exception of *am*85, *am*54, and *r*67, the relative order of the markers indicated in the map was established previously by two- and three-factor crosses.[4,11-13] We now find that *am*54 is closely linked to *r*67 (1.5% recombinants), and *am*85 is closely linked to *tu*42b (3.5% recombinants). The order *tu*44—*am*85—*am*54 is established by means of the three-factor cross *tu*44 *am*54 × *am*85 (cross 14, Table 1). The order *tu*44—*tu*42b—*r*67 is confirmed by cross 15, Table 1.

The information cited above is compatible with either of two alternatives. The linkage map may have ends, in which case *r*67 lies closer to *ac*41 than to *h*42, as represented in Figure 1. Or the linkage map could be a circle formed by joining the ends shown in Figure 1, in which case *r*67 would be expected to lie closer to *h*42 than to *ac*41.

The cross *r*67 *h*42 *ac*41$^+$ × *r*67$^+$ *h*42$^+$ *ac*41 (cross 1, Table 1) distinguishes between these alternatives. The progeny of the cross were plated under conditions that permitted the recognition of the *h*42 *ac*41 recombinants. About 65 per cent of these were *r*, and 35 per cent *r*$^+$, showing that the *r* marker is more closely linked to *h* than to *ac*. In other words, the results of cross 1 are inconsistent with previous data summarized in Figure 1 unless the linkages are represented on a circle.

The same linkage was tested in cross 2, Table 1, with a different arrangement of the parental markers. The results are consistent with those of cross 1, showing that the marker frequencies depend on linkages between loci only, and do not reflect a bias associated with particular markers.

Additional three-factor and four-factor crosses are listed in Table 1. They are similar in principle to crosses 1 and 2 and place all the markers in a unique order on a circular map. In some crosses, unequal multiplicities of infection were used to increase the sensitivity of the linkage tests.[4] In all crosses except 3, 14, and 15, the frequency of recombinants was measured among the early phage progeny (1–10 per bacterium), and usually the drift toward genetic equilibrium of unselected alleles was demonstrated by additional sampling at later times during phage growth. Arguments concerning the validity of these types of linkage test have been presented by Streisinger and Bruce.[4] Scoring procedures are described in Table 2. Figure 2 identifies linkages tested in the individual crosses and summarizes the circular map with which all results are consistent.

Discussion.—Our results demonstrate genetic circularity and are thus compatible with the model presented in the introduction to this paper. The circularity of the

TABLE 1

No.	Cross: Parent 1				Parent 2				Multiplicity: Parent 1	Multiplicity: Parent 2	Progeny Phage: Recombinant ratio measured*	Progeny Phage: Value of ratio	Progeny Phage: Control ratio	Progeny Phage: Value of control ratio
1	*r*67	*h*42	+		+	+	*ac*41		9.8	10.3	112/·12	0.65	1../...	0.53
2	+	*h*42	+		*r*67	+	*ac*41		7.5	7.4	112/·12	0.66	1../...	0.54
3	+	*ac*41	*r*EDb48		*h*42	+	+		4.2	4.7	112/·1·	0.09		
											211/·1·	0.11		
											212/·1·	0.02		
4	*r*67	*r*73	+		+	+	*r*47		5.0	0.5	221/·21	0.58		
5	+	+	*r*47		*r*67	*r*73	+		3.1	0.7	212/·12	0.33		
6	+	*r*73	+		*r*67	+	*r*47		5.8	0.6	221/·21	0.53		
7	*r*67	+	*r*47		+	*r*73	+		5.1	0.7	212/·12	0.29		
8	*r*73	+	+		+	*r*47	*r*48		8.6	0.9	212/21·	0.29		
9	+	*r*47	*r*48		*r*73	+	+		7.2	0.8	122/12·	0.43		
10	*r*73	+	*r*48		+	*r*47	+		8.6	0.8	212/21·	0.27		
11	+	*r*47	+		*r*73	+	*r*48		8.4	0.9	122/12·	0.40		
12	*r*48	+	*tu*44		+	*tu*45	+		8.8	9.6	112/·12	0.74	1../...	0.60
13	+	+	*tu*44	—	*r*48	*tu*45	+		7.5	7.4	112/·12	0.72	1../...	0.55
14	*tu*44	+	*am*54		+	*am*85	+		6	6	112/·12	0.80		
15	+	*tu*42	*r*67		*tu*44	+	+		6.3	7.8	122/12·	0.74		
16	*r*48	+	*am*54	*tu*41	+	*am*85	+	+	7.1	7.6	2121/·12·	0.12	2.../....	0.53
											212·/·12·	0.46		
											·121/·12·	0.36		
17	*r*48	*am*85	+	*tu*41	+	+	*am*54	+	9.7	9.4	1212/·21·	0.13	2.../....	0.54
											121·/·21·	0.46		
											·212/·21·	0.37		

* 1 or 2 indicates a marker derived from parent 1 or 2, and a dot (·) indicates a marker derived from either parent. The ratio 112/·12 in cross 1, for instance, represents *r*67 *h*42 *ac*41/(*r*67 *h*42 *ac*41 plus r^+ *h*42 *ac*41).

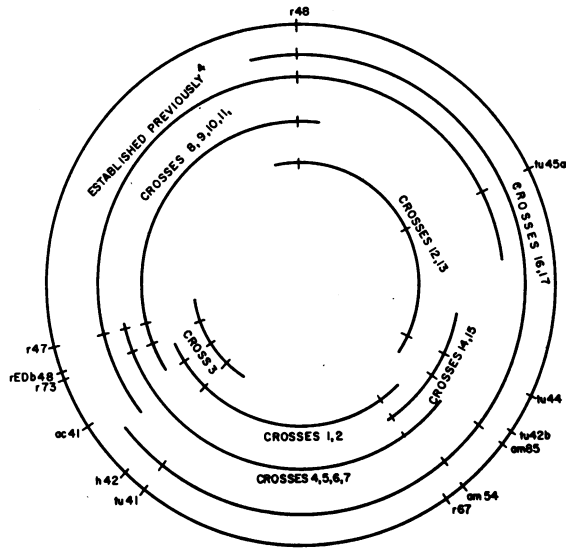

FIG. 2.—The circular map of T4. The locations of markers used for any one cross are connected by an arc.

genetic map of T4 has been confirmed by two-factor crosses made with a large set of amber mutants[15] and temperature-sensitive mutants.[16] Foss[17] has been able to demonstrate genetic circularity in T4 by means of a single, ingeniously devised four-factor cross.

TABLE 2

PROCEDURES FOR SCORING THE PROGENY OF CROSSES

Crosses	Plates	Bacteria	Scoring
1, 2	Salt-poor EHA with acriflavin	Phage preadsorbed to S/6, plated on a mixture of K/4 and S/6	Only *h*42 *ac*41 forms clear plaques, classified as *r* or r^+ by inspection.
3	EHA with acriflavin	Mixed K/4 and S/6	Only *ac*41 forms plaques, classified as *r* or r^+ and *h* or h^+ by inspection.
4–11	Tryptone	K12(λ)	Only $r73^+$ $r47^+$ forms plaques, classified as *r* or r^+ by inspection.
12, 13	EHA	S/6	$tu45^+$ $tu44^+$ plaques selected and classified as *r* or r^+ by inspection.
15	EHA	S/6	Genotypes tu^+ r^+ and tu^+ *r* classified by inspection.
14, 16–17	EHA	S/6	Only am^+ forms plaques, classified as *r* or r^+ and *tu* or tu^+ by inspection.

It should be emphasized that our results, while demonstrating genetic circularity, are by no means a critical test of the model we present; a number of other models would account for the results equally well. For instance, Stahl[18] has pointed out that a circular genetic map would be obtained if the chromosome were a nonpermuted rod and if genetic exchanges frequently occurred in pairs. A decision with respect to the molecular basis of circularity calls for other, more critical tests.

Summary.—The linkage map of phage T4 is circular.

The authors wish to acknowledge their great indebtedness to F. W. Stahl, without whose encouragement they would not have taken their rather bizarre notions seriously. Many of the fea-

tures of the proposed model were developed in the course of conversations and correspondence with F. W. Stahl, M. Meselson, and M. Fox.

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[9] P. F. Davison, D. Freifelder, and B. W. Holloway [*J. Mol. Biol.*, **8**, 1 (1964)] obtained physical evidence suggesting that the strands are not continuous. Thus, the question of strand interruptions is not yet resolved. Although it is true that our experiments were motivated by Berns and Thomas' conclusions and are compatible with them, they do not in fact have any direct bearing on the question of whether strand interruptions do exist.

[10] Particular models for the generation of a population of circularly permuted chromosomes will be discussed in detail in a subsequent communication. The following two alternatives may help to clarify the present discussion: (1) the ends of a particular chromosome, after its injection into a bacterium, could be imagined to pair and to join, forming a circular structure. This circle might then be opened by cuts in the two chains of the DNA molecule, the cuts being staggered in relation to each other. (2) The chromosome could be imagined to replicate and the progeny chromosomes to join end-to-end at the region of terminal redundancy. The polymers thus formed would have to be cut into phage-sized pieces before maturation

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H^3-THYMIDINE UPTAKE BY A RING X CHROMOSOME IN A HUMAN FEMALE

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The use of H^3-thymidine to label cultures of peripheral leukocytes has revealed a marked asynchrony in the replication of one chromosome in the normal human female.[1-4] The hypothesis that this chromosome, which labels late in the period of DNA synthesis, is one of the two X chromosomes, is supported by the finding of three late-labeling chromosomes in males with the karyotype XXXXY,[5-7] four late-labeling chromosomes in a female XXXXX,[8] and one large late-labeling chromosome in patients with gonadal dysgenesis and the karyotype XX_I,[8-11] where the